Kunutsor, S. K., Whitehouse, M. R., Blom, A. W., & Laukkanen, J. A. (2017). Low serum magnesium levels are associated with increased risk of fractures: a long-term prospective cohort study. European Journal of Epidemiology. DOI: 10.1007/s10654-017-0242-2

APPENDIX SUPPLEMENTS

Low serum magnesium levels are associated with increased risk of fractures: A long-term prospective cohort study

Appendix 1	STROBE 2007 Statement—Checklist of items that should be included in reports of cohort studies
Appendix 2	Baseline participant characteristics by quartiles of serum magnesium
Appendix 3	Hazard ratios for incident femoral fractures by quartiles of serum magnesium levels
Appendix 4	Association of serum magnesium and incident fractures by quartiles of serum magnesium (with quartile 1 as a reference comparison)

Appendix 1: STROBE 2007 Statement

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Page 1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	Page 2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Page 3-4
Objectives	3	State specific objectives, including any prespecified hypotheses	Page 3-4
Methods			
Study design	4	Present key elements of study design early in the paper	Study Design and Participants
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Study Design and Participants
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	Study Design and Participants
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	Not applicable
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Risk Factor Assessment
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Risk Factor Assessment
Bias	9	Describe any efforts to address potential sources of bias	Statistical Analyses
Study size	10	Explain how the study size was arrived at	Statistical Analyses
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Statistical Analyses
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	Statistical Analyses
		(*b*) Describe any methods used to examine subgroups and interactions	Statistical Analyses
		(*c*) Explain how missing data were addressed	Not applicable
		(*d*) If applicable, explain how loss to follow-up was addressed	Not applicable

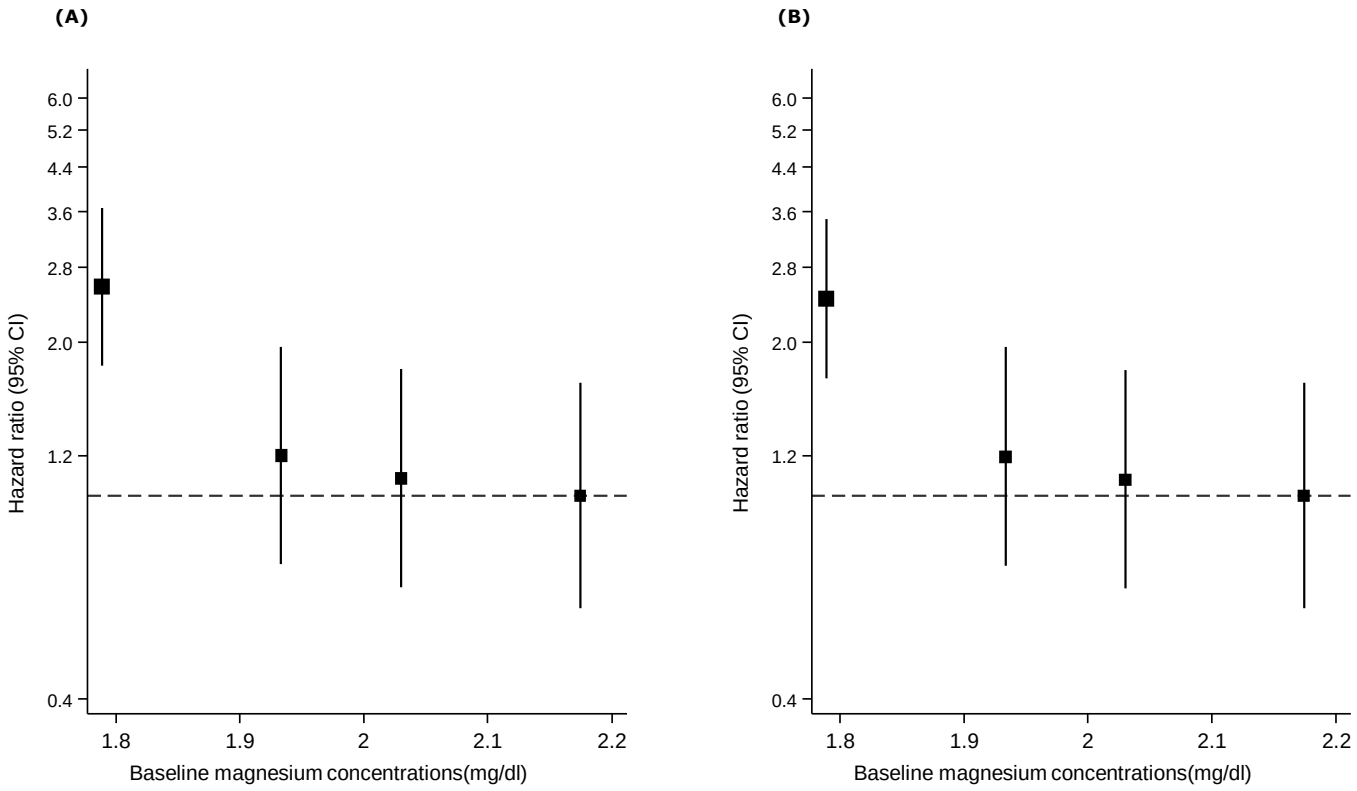
		(*e*) Describe any sensitivity analyses	Statistical Analyses
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Study population
		(b) Give reasons for non-participation at each stage	Study population
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Results; Table 1; Appendix 2
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) Summarise follow-up time (eg, average and total amount)	Results
Outcome data	15*	Report numbers of outcome events or summary measures over time	Results
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Results; Tables 2-4
		(*b*) Report category boundaries when continuous variables were categorized	Results; Tables 2-4
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Results; Figure 2
Discussion			
Key results	18	Summarise key results with reference to study objectives	Discussion - Summary of main findings
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Discussion
Generalisability	21	Discuss the generalisability (external validity) of the study results	Discussion
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Page 16

Appendix 2. Baseline participant characteristics by quartiles of serum magnesium

	Quartile 1 Mean (SD), median (IQR), or n (%)	**Quartile 2 Mean (SD), median (IQR), or n (%))**	**Quartile 3 Mean (SD), median (IQR), or n (%)**	**Quartile 4 Mean (SD), median (IQR), or n (%)**	***P*-value**
Magnesium (mg/dl)	1.79 (0.09)	1.93 (0.03)	2.03 (0.3)	2.17 (0.08)	< 0.0001
Questionnaire/Prevalent conditions					
Age at survey (years)	53.1 (5.5)	52.4 (5.7)	53.3 (4.8)	53.7 (3.9)	0.0002
Alcohol consumption (g/week)	86.8 (170.8)	78.9 (154.8)	71.6 (101.1)	66.0 (110.3)	0.063
Total energy intake, kJ/day	9,998 (2,736)	9,900 (2,676)	9,871 (2,557)	9,647 (2,450)	0.143
Socioeconomic status	8.70 (4.09)	8.46 (4.24)	8.60 (4.30)	8.26 (4.33)	0.339
Dietary magnesium intake (mg/day)	419.4 (72.2)	419.6 (69.7)	417.2 (64.3)	412.3 (70.8)	0.266
History of diabetes					
No	527 (93.1)	534 (95.7)	551 (97.7)	544 (97.7)	
Yes	39 (6.9)	24 (4.3)	13 (2.3)	13 (2.3)	< 0.001
Smoking status					
Other	384 (67.8)	389 (69.7)	374 (66.3)	382 (68.6)	
Current	182 (32.2)	169 (30.3)	190 (33.7)	175 (31.4)	0.665
History of hypertension					
No	387 (68.4)	387 (69.4)	394 (69.9)	396 (71.1)	
Yes	179 (31.6)	171 (30.7)	170 (30.1)	161 (28.9)	0.796
Physical measurements					
BMI (kg/m^2)	27.2 (3.8)	26.7 (3.5)	27.0 (3.5)	26.9 (3.5)	0.209
Height (cm)	173.0 (6.1)	172.9 (6.3)	172.9 (6.3)	172.5 (6.2)	0.560
SBP (mmHg)	134 (17)	134 (16)	134 (17)	134 (18)	0.931
DBP (mmHg)	89 (11)	88 (10)	89 (10)	88 (11)	0.513
Physical activity (kj/day)	1,500 (1,414)	1,596 (1,658)	1,547 (1,370)	1,540 (1,502)	0.760
Lipid markers					
Total cholesterol (mmol/l)	5.82 (1.13)	5.82 (1.10)	5.93 (1.02)	6.06 (1.05)	0.0002
HDL-C (mmol/l)	1.31 (0.33)	1.29 (0.29)	1.29 (0.28)	1.28 (0.29)	0.485
Triglycerides (mmol/l)	1.08 (0.79-1.53)	1.08 (0.79-1.52)	1.11 (0.80-1.57)	1.12 (0.83-1.64)	0.118
Metabolic and renal markers					
Fasting plasma glucose (mmol/l)	5.73 (1.96)	5.25 (0.96)	5.24 (0.79)	5.22 (0.94)	< 0.0001
Serum creatinine (µmol/1)	87.2 (15.3)	89.1 (14.3)	89.9 (12.5)	92.7 (34.8)	0.0002
Estimated GFR (ml/min/1.73 m^2)	90.1 (17.7)	87.7 (15.7)	86.1 (19.0)	84.0 (15.7)	< 0.0001
Trace elements					
Serum zinc (mg/l)	0.92 (0.13)	0.94 (0.12)	0.94 (0.11)	0.95 (0.12)	0.0006
Serum ionized calcium (mmol/l)	1.18 (0.05)	1.18 (0.05)	1.18 (0.05)	1.18 (0.05)	0.016
Serum potassium (mmol/l)	3.93 (0.28)	3.93 (0.37)	3.92 (0.27)	3.90 (0.29)	0.171

BMI, body mass index; CHD, coronary heart disease; CI, confidence interval; DBP, diastolic blood pressure; GFR, glomerular filtration rate; HDL-C, high-density lipoprotein cholesterol; IQR, interquartile range; SD, standard deviation; SBP, systolic blood pressure;

Appendix 3. Hazard ratios for incident femoral fractures by quartiles of serum magnesium levels



A, adjusted for age; **B**, adjusted for age, body mass index, height, systolic blood pressure, smoking status, history of diabetes, alcohol consumption, and physical activity; the mean magnesium level (mg/dl) was 1.79 for the lowest quartile; 1.93 for the second quartile; 2.03 for the third quartile; and 2.17 for the top quartile; CI, confidence interval

Appendix 4. Association of serum magnesium and incident fractures by quartiles of serum magnesium (with quartile 1 as reference comparison)

Serum magnesium(mg/dl)	Events/ Total	Model 1		Model 2		Model 3	
		HR (95% CI)	*P*-value	HR (95% CI)	*P*-value	HR (95% CI)	*P*-value
Total fractures							
Q1 (0.92-1.88)	46 / 566	ref		ref		ref	
Q2 (1.88-1.98)	27 / 558	0.53 (0.33 to 0.86)	0.010	0.55 (0.34 to 0.89)	0.015	0.56 (0.35 to 0.91)	0.019
Q3 (1.98-2.08)	24 / 564	0.44 (0.27 to 0.72)	0.001	0.46 (0.28 to 0.76)	0.002	0.48 (0.29 to 0.79)	0.004
Q4 (2.08-2.55)	26 / 557	0.48 (0.29 to 0.77)	0.003	0.50 (0.31 to 0.82)	0.005	0.56 (0.34 to 0.91)	0.019
Femoral fractures							
Q1 (0.92-1.88)	31 / 559	ref		ref		ref	
Q2 (1.88-1.98)	16 / 553	0.47 (0.26 to 0.86)	0.014	0.49 (0.27 to 0.90)	0.022	0.51 (0.27 to 0.94)	0.031
Q3 (1.98-2.08)	16 / 556	0.42 (0.23 to 0.77)	0.005	0.44 (0.24 to 0.81)	0.009	0.47 (0.26 to 0.87)	0.017
Q4 (2.08-2.55)	15 / 556	0.39 (0.21 to 0.73)	0.003	0.41 (0.22 to 0.77)	0.005	0.47 (0.25 to 0.88)	0.019

CI, confidence interval; HR, hazard ratio; ref, reference; Q, quartile

Model 1: Adjusted for age

Model 2: Model 1 plus body mass index, height, systolic blood pressure, smoking, history of diabetes, alcohol consumption, and physical activity

Model 3: Model 2 plus estimated glomerular filtration rate, socioeconomic status, total energy intake, serum zinc, serum potassium, and serum ionized calcium